school in every region of the Health Service. I am sure that it would not be very difficult to draw up a programme so that the junior staff working in peripheral hospitals could attend regularly postgraduate lectures and demonstrations in the nearest medical school. Provision of such facilities for further training would attract doctors in the hospital service and benefit both sides of the service. —I am, etc.,

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New Clinical Schools

SIR,—I can readily sympathize with those Brighton warriors Dr. S. P. Hall-Smith and Dr. R. I. K. Elliott battling for a new medical school (29 October, p. 1071), although I have considerable reservations about the suggestions of Dr. Malleson on how it might be organized. I write, nevertheless, to question what they boldly represent as fact. They write that "there is a surplus of suitably qualified school leavers who cannot obtain acceptance by a medical school." The fact is that we do not know whether this statement is true or not. We shall not know the facts until after next autumn, when the Universities Central Council for Admissions will have, for the first time, the figures for the whole country. I have a sneaking feeling, however, that the number of the suitably qualified to be disappointed will be found to be very few. On the other hand, there are many suitably qualified, or who could be so qualified, who do not seek a place in medicine. The reasons for this are many and some only too obvious. Let medicine once more be seen to be the interesting life which it is, let the various "charters" be fulfilled and there will be no more shortage of the suitably qualified. —I am, etc.,

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Blood Transfusion and Infectious Hepatitis

SIR,—There are at present no specific tests for virus hepatitis, but the serum transaminase levels have proved a sensitive index of liver damage, particularly the ratio of serum glutamic oxaloacetic transaminase to serum glutamic pyruvic transaminase.[1,2] These tests have not been carried out in the small series of patients reported by Dr. J. Shafar and Dr. J. P. Midgley (22 October, p. 1009), and it should be difficult to draw any valid conclusions from their results on the absence of anicteric post-transfusion hepatitis in 82 patients who received 222 pints of blood. Moreover, it is hazardous and misleading to attempt to translate these results into national figures. Estimates of the risk of hepatitis in blood recipients in the U.S.A. vary from 0.3 to 4.13%, and from a number of reports it was estimated that the over-all mortality from post-transfusion hepatitis could be as high as 27.5%. Even more significant is the fact that although infectious hepatitis cannot be considered a major cause of death it nevertheless ranked in 1959 in the U.S.A. second only to influenza among the deaths attributed to acute virus infections.

In this country an estimate of the size of the problem of hepatitis cannot be made, since hepatitis is not notifiable on a national basis. Nevertheless, it should be a matter for considerable anxiety that there are indications that the number of deaths from hepatitis after cardiac surgery in some centres exceeds the mortality from surgery. Therefore, before we can aspire to undertake any preventive measures the first step should be the notification of hepatitis and the establishment of a follow-up system for all patients who have received blood transfusion. The problem is surely of such importance as to preclude any attempts to guess the actual figures for hepatitis.

The incidence of post-transfusion hepatitis can be significantly reduced by the judicious selection of patients for transfusion by the avoidance of the one- or two-pint transfusion of whole blood, by the concurrent administration of gammaglobulin to high risk patients —for example, cardiac surgery, artificial dialysis—or by the use of hepatitis-free plasma. The supply of human gammaglobulin cannot at present allow its free use with every blood transfusion. At the same time the current schedules of administration of gammaglobulin require more precise definition. The use of suitable preparations of gammaglobulin mixed with the donated blood before transfusion merits close investigation.—I am, etc.,

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Prescribing Costs

SIR,—As manufacturers of Panadol we would like to give Dr. R. J. Dinsmore (8 October, p. 891) the explanation he requests.

More than a decade ago we concluded that *N*-acetyl-*p*-aminophenol, a substance which had been synthesized many years previously and was, therefore, unpatentable, was likely to possess superior analgesic properties. Subsequent clinical investigation confirmed our belief, and after elaborating what we considered to be adequate standards for its pharmaceutical presentation we introduced Panadol tablets. No batch of tablets was released, nor is it today, without passing 92 control analyses during manufacture. During the next few years, as a result of our technical information programme, physicians confirmed our claims in practice and Panadol became one of the most widely prescribed analgesics.

As is common when a research-based pharmaceutical company has created a demand for a substance which is unpatented, copy products soon appeared. Such preparations were rightly cheaper than Panadol, because the firms producing them had not incurred the same research, development, introduction, reaction monitoring, and other expenses. The copyists were not maintaining a long-term research programme aimed at providing even better analgesics. Many were not expensively engaged in building an export business. Moreover, the copy products were not identical with Panadol.

Not until 1963 did a monograph appear, setting standards for the manufacture of paracetamol tablets. Even then the *B.P.* specification implied only 32 control tests, compared with Panadol's 92. Naturally, we could not reduce the standards for Panadol upon which physicians had come to rely. Furthermore, we were, as we are today, continuing our research programme and gaining exports. The price of Panadol has always justified its price under the Voluntary Price Regulation Scheme agreed between the industry and the Ministry of Health. The price has been reduced five times and currently is 35% *lower* than at the time of introduction. During the period retail prices have *risen* by 35%.

There is a prevalent tendency to refer to pharmaceutical preparations in terms of their active chemical ingredients. Particle size, excipients, compression pressures, *p*H, contaminants, quality control, and the like are disparagingly dismissed as "pharmaceutical elegance." Such factors can and do have considerable therapeutic significance, as the literature testifies. Gwilt *et al.*[1] were able to show, after the *British Pharmacopoeia* monograph had appeared, that there were marked differences in blood levels following the ingestion of paracetamol tablets produced by different manufacturers.

The prices that we can obtain in export markets are inevitably linked with those that rule at home. A saving of a few thousand pounds to the N.H.S. can literally cost tens of thousands of pounds in foreign currency earnings. Most of the advances in therapeutics have come from research-based pharmaceutical companies. This research can only be financed out of current profits. There are no subsidies. And because of the lead-time and competition even the patented discoveries of today are the "standard" drugs of less than 10 years hence. A dogmatic or misinformed determination to enforce a "cheap drugs" policy could, with a loss of quality, result in a short-term economic gain. Inevitably it would cripple British research and exporting activity and in the long run would result in higher prices having to be paid for advances in therapeutics made abroad.—I am, etc.,

C. R. B. WILLIAMSON, Managing Director.

Bayer Products Company, Surbiton.

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Burkitt's Tumour in Pregnancy

SIR,—I wish to report an unusual case of Burkitt's tumour in pregnancy. The patient was a 36-year-old Nigerian woman, first seen nine days after the delivery of her sixth infant.

She presented with enormous painful swelling of both breasts (Fig. 1) with no secretion, pyrexia, and increasing muscular weakness. On admission her temperature was 102° F., she had signs of right facial nerve palsy, and was too weak to walk. There were sibilant rhonchi in both upper zones of the chest, the pulse was 136 per minute, and blood pressure 145/60 mm. Hg. Investigation showed haemoglobin 10 g./100 ml.;

W.B.C. 13,800/cu. mm. with polyleucocytosis and shift to the left. There were no malarial parasites. Sputum showed scanty pus cells, no tubercle bacilli, and chest *x*-ray showed no active disease. She was treated with antimalarials and tetracyclines for seven days, but her temperature remained between 100 and 102.4° F. Breast enlargement was unaffected

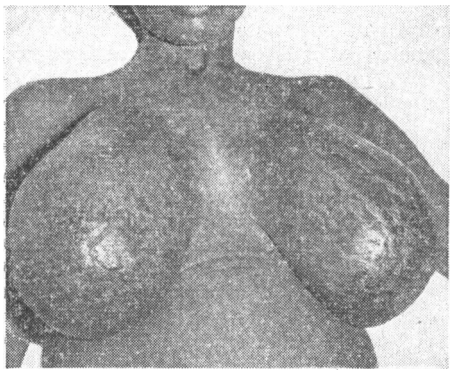

FIG. 1.—Burkitt's tumour of breasts, showing massive enlargement, shiny skin, with patches of desquamation.

by methyl testosterone 5 mg. daily. On the fifteenth day after admission her condition deteriorated; she became semicomatose and died three hours later.

At post mortem some thickening of the roots of the 5th, 6th, and 7th cranial nerves was observed, and slight enlargement of the pituitary gland. The tissue of both breasts was replaced by massive white tumours (Fig. 2) and there were multiple nodules of

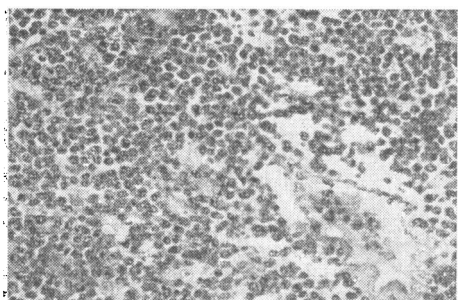

FIG. 2.—Burkitt's tumour of breast, showing sheets of blast cells with scattered pale histiocytes present, giving the typical "starry sky" appearance. (H. and E. ×400.)

tumour in both axillary tails. Lymphatic glands at the root of the right lung were replaced by white tumour tissue, which extended up the tracheal wall for 3 cm. There was a white tumour deposit in the cortical area of the right kidney.

Histological examination revealed typical Burkitt's tumour in the breast, uterus, pituitary, mediastinal glands, and brain. The brain lesion is of interest—there was infiltration of the meninges and marked perivascular cuffing of vessels by malignant cells—the picture being that of a "Burkitt meningoencephalitis."

The relatively short history in this patient, whose symptoms first appeared at eight months' gestation, her rather advanced age, and the gross breast involvement suggests possible lowering of immunity, or increased susceptibility in association with pregnancy. Such a phenomenon has been observed in amoebiasis in pregnancy,[1] and similarly in cases of pneumococcal meningitis of pregnant and puerperal Nigerian women.[2]—I am, etc.,

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Osteoarthrosis after Poliomyelitis

SIR,—We were interested in Mr. D. R. Sweetnam's comments (8 October, p. 888) on our findings that the incidence of degenerative joint disease seems to be diminished following poliomyelitis. The assertions which he makes, to the effect that muscle stresses may be responsible for the development of joint pathology, seem of such fundamental importance when considering the aetiology of osteoarthrosis that we would like to know the source of the evidence on which they are based. In the absence of such conclusive evidence we feel that an alternative interpretation is at least as likely to be correct. Thus, it would seem to us that correctly balanced muscle forces across a joint, however strong, must be *physiological* and should *protect* the joint surfaces and surrounding ligaments from abnormal stresses and strains. If this were not so, the incidence of degenerative joint disease would be even higher than it already is.

Structural abnormalities of joints—whether congenital or acquired—are recognized as predisposing to osteoarthrosis. It has been assumed that this is because of *abnormal* forces acting on the joint and allowing excessive friction in unphysiological areas of the joint surfaces. We felt that a similar situation was probably operating in the case of paretic joints in which not only asymmetrical muscle pulls but abnormal torsional strains are operative. It is for this reason that we were surprised at the low incidence of reactive changes in the joints which we studied and even more surprised by the low incidence of symptoms arising from strains of the ligaments and surrounding soft tissues. Furthermore, as we pointed out, "neurogenic joints" may be associated with instability and frequently with muscle weakness, but they certainly are not spared the ravages of arthrosis. Any interpretation of our findings must take this fact into account.

If indeed Mr. Sweetnam is correct in his interpretation, then it would seem to us that the attempt to redevelop muscles controlling damaged joints—which is the universal prescription of orthopaedic and physical medicine specialists—would involve the risk of *increasing* rather than decreasing the damage to the joints and should therefore cease forthwith!—We are, etc.,

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Medication Marker

SIR,—Drs. I. H. Jones and F. J. J. Letemendia write describing the use of riboflavine as a tablet marker (15 October, p. 948), but they fail to mention relevant papers, which to some extent anticipate their letter.[1–5] I agree that the vitamin has merits as a marker, but certain aspects of their work must be criticized:

(1) They do not stress sufficiently the importance of the influence of the specific gravity of the urine specimen on its fluorescent properties. Using myself as a subject, and taking doses of 6 mg. of riboflavine, I found that specimens with a specific gravity of less than 1005 were very variable in their fluorescent behaviour. The consistent results obtained by the authors with early morning specimens were due to the high concentration of urine excreted overnight.

(2) Their suggestion that urine testing should be a disciplinary measure to enforce conformity by their patients is surprising. Surely a daily confrontation of doctor, patient, urine, and torch would be so bizarre as to introduce an unpredictable and unacceptable variable into a trial. Further it would be practical only with an inpatient trial, and it is the unsupervised outpatient who presents the real problem.

(3) The authors lay too much stress on the use of tablet markers at the expense of a discrete method of observing tablet consumption, such as I have described.[5] Searching the urine can yield only "glimpses" concerning the conformity of the patient; assessing the tablet consumption gives an overall estimate of the adherence to a schedule.

(4) The authors seem unaware that "riboflavine affects the action of phenothiazines"[6]; that there may be competition between phenothiazines, biogenic amines, and riboflavine for active sites.[7] This is a great nuisance, and must be allowed for in the design of any trial involving a marked psychotropic drug.—I am, etc.,

Camberley,
Surrey. A. M. W. PORTER.

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Open Door Chest Clinic

SIR,—In his interesting article (6 August, p. 351) on the "open door" *x*-ray department, Dr. P. L. Cook describes 1,233 chest examinations, comprising almost half the year's total. He indicates that follow-up films were arranged . . . "to check resolution of an inflammatory process or re-expansion following a pneumothorax . . . and . . . of patients who had a known tuberculous history, or had recently been discharged from hospital having had a chest illness or a post-operative chest complication." He lists 90 instances of "collapse and/or consolidation," 39 cases of tuberculosis, 27 of emphysema, and 18 of long-standing inflammatory disease.

All this suggests a comprehensive chest surveillance and diagnosis service. But one must inquire further about the problems of communication and reporting techniques to which Dr. Cook refers; for it is the general practitioner, with the patient at his side and the radiologist's report in his hand, who must make a clinical decision. Is the open access